Randomized Clinical Trial of Different Bandage Regimens after Foam Sclerotherapy for Varicose Veins

O'Hare JL, Stephens J, Parkin D, et al. Br J Surg 2010;97:650-6.

Conclusion: There are no differences between sclerotherapy results in patients treated for truncal varices with foam sclerotherapy regardless of whether compression therapy after the procedure is used for 1 or 5 days.

Summary: There are no data on the optimal bandaging regimen after foam sclerotherapy for truncal varices. In Great Britain, 80% of the members of the Vascular Society of Great Britain and Ireland responding to a questionnaire, and who treated patients with sclerotherapy, indicated they used compression bandages, and 90% subsequently used compression stockings after compression bandaging. Duration of treatment ranged from 1 to 7 days for initial bandages, with compression stockings used for 7 to 14 days, with some surgeons recommending compression stockings for up to 3 months. The authors sought to determine whether duration of bandaging could be reduced after foam sclerotherapy for truncal varices.

Patients with primary uncomplicated varicose veins were randomized after foam sclerotherapy treatment to wearing compression bandaging for 24 hours or 5 days. In each case after compression bandages were removed, thromboembolism deterrent (TED) stockings then used for a total of 14 days of compression after foam sclerotherapy. The primary end point of the study was the 6-week Aberdeen Varicose Vein Severity Score (AVVSS) and Buford pain score. The study randomized 124 legs, of which 61 were randomized to 24 hours of compression bandaging and 63 to 5 days of compression bandaging. Venous occlusion rates at 6 weeks were 90% and 89%, respectfully ($P = .842$). There were no differences in phlebitis after 2 weeks ($P = .445$), skin discoloration after 6 weeks (46% vs 40%; $P = .546$). There were no differences between groups in the AVVSS from baseline to 2 weeks (−0.29 vs −0.80; $P = .717$) or to 6 weeks (−5.89 vs −5.14; 95% confidence interval [CI] for the difference, −3.29 to 1.8; $P = .563$). There were also no differences between groups in changes in the Buford pain score from baseline to 2 weeks (−9.04 vs −2.80, $P = .248$) or to 6 weeks (−17.32 vs −8.46; 95% CI for the difference, −19.06 to 1.33; $P = .088$). Finally, the two groups also did not demonstrate any differences in changes in the Short Form-36 score from baseline to 6 weeks (2.02 vs. 1.74; $P = .903$).

Comment: Foam sclerotherapy is replacing liquid sclerotherapy as the preferred method of sclerotherapy for patients with truncal varicosities. Compression after treatment is essential to optimal results. However, as the authors point out with respect to foam sclerotherapy, the optimal duration of compression after treatment has not been adequately studied. This study is good news for patients. Compression bandages are not comfortable, and the results indicate that 24 hours of compressive bandaging, followed by a TED stocking for a total of 2 weeks, is just as efficacious as 5 days of compressive bandaging, followed by a TED stocking for a total of 2 weeks. The study provides practical guidance for post-therapy bandaging of patients undergoing foam sclerotherapy.

Randomized Controlled Trial of Dual Antiplatelet Therapy in Patients Undergoing Surgery for Critical Limb Ischemia

Burdess A, Nimmo AF, Garden OJ, et al. Ann Surg 2010;252:37-42.

Conclusion: Dual antiplatelet therapy of aspirin and clopidogrel compared with aspirin alone in patients undergoing surgery for critical limb ischemia reduces biomarkers of thrombosis without an increase in unacceptable bleeding.

Summary: Myocardial injury is common after vascular surgery, with reported incidences of between 8% and 40%. In patients with vascular disease, use of clopidogrel has a moderate additional secondary preventative effect to that of aspirin for prevention of cardiovascular end points (Bhatt DL, N Engl J Med 2006;354:1706-717 and Yusuf S, et al, N Engl J Med 2001:345:494-502). The authors reasoned that given the benefits of dual antiplatelet therapy, it would be reasonable to postulate dual antiplatelet therapy would be beneficial in patients undergoing vascular surgery. The hypothesis was that perioperative dual antiplatelet therapy would improve biomarkers of atherothrombosis in patients undergoing surgery for critical limb ischemia without causing unacceptable bleeding. This was a double-blind, randomized, controlled trial comprising 108 patients undergoing amputation or infrainguinal revascularization for critical limb ischemia. All patients were maintained on aspirin (75 mg daily) and then randomized to clopidogrel (600 mg before surgery and 75 mg daily for 3 days) or placebo. There were 50 patients in the clopidogrel group and 58 in the placebo group. Myocardial injury was assessed by plasma troponin concentrations and platelet activation assessed by flow cytometry.

Platelet-monocyte aggregation before surgery was reduced by clopidogrel (38%-30%; $P = .007$). This reduction was retained postoperatively ($P = .0019$). Postoperatively, there were 18 troponin events, 8 (16%) in the clopidogrel group vs 10 (17.2%) in the placebo group (relatively risk [RR] 0.93, 95% confidence interval [CI], 0.39-2.17, $P = .86$). Half of the troponin-positive events occurred preoperatively. Clopidogrel was associated with a greater decline in troponin concentrations ($P = .001$). Blood transfusions were increased in the clopidogrel group (28% vs 12.6%; RR, 2.3; 95% CI, 1.0-5.29; $P = .037$). There was, however, no increase in major life-threatening bleeding (RR, 1.4; 95% CI, 0.49-3.76; $P = .56$) or minor bleeding (RR, 1.64; 95% CI, 0.87-3.1; $P = .12$).

Comment: This is the first double blind, randomized trial of perioperative dual antiplatelet therapy in patients undergoing surgery for critical limb ischemia. The study was underpowered to detect a difference in clinical events; however, the authors were able to demonstrate improvements in biomarkers of platelet activation without an increase in bleeding complications. Many troponin-positive events occurred before surgery. This suggests "silent" preoperative myocardial injury is common in patients with critical limb ischemia. The study indicates potential benefits of dual antiplatelet therapy in the perioperative period in patients with critical limb ischemia. Whether improvements in surrogate biomarkers translate to clinical benefit remains to be established.

Risk of Recurrent Venous Thrombosis in Homozygous Carriers and Double Heterozygous Carriers of Factor V Leiden and Prothrombin G20210A

Lijfering WM, Middeldorp S, Veeger NJ, et al. Circulation 2010;121:1706-12.

Conclusion: Patients with venous thromboses who are homozygous for factor V Leiden and/or prothrombin G20210A or are double heterozygous carriers of factor V Leiden and prothrombin G20210, do not have a high risk of recurrent venous thrombosis.

Summary: Within the Caucasian population, factor V Leiden has a prevalence of approximately 5% and the prothrombin G20210A mutation has a prevalence of approximately 2%. The risk for initial venous thrombosis is clearly higher in heterozygote and homozygote carriers of factor V Leiden and prothrombin G20210A. Heterozygote carriers of factor V Leiden have an approximately a 5-fold increased risk for initial venous thrombosis, whereas homozygote carriers have an 18-fold increased risk for initial venous thrombosis. Individuals heterozygous for both factor V Leiden and prothrombin G20210A have approximately a 20-fold risk for initial venous thrombosis. It is generally assumed that patients with thrombophilia on the bases of factor V Leiden and/or prothrombin G20210A mutations would also have increased risk for recurrent venous thrombosis. This assumes the risk of recurrence is driven primarily by the same factors that prompted the initial venous thrombosis. However, some studies have suggested thrombophilia secondary to factor V Leiden and prothrombin G20210A mutations actually do not increase the risk of recurrent venous thrombosis. This would argue against testing for these genetic defects in individuals with an unprovoked first-time venous thrombosis (Christansen SC et al, JAMA 2005;293; 2352-61; and Baglin T et al, Lancet 2003;362:523-6).

The authors performed a case-control study using a large cohort of families with thrombophilia identified through three major university hospitals in the Netherlands. The goal was to calculate the risk of recurrent venous thrombosis in individuals with homozygosity or double heterozygosity of factor V Leiden and/or prothrombin G20210A. Controls were patients with only one episode of venous thrombosis, and cases were individuals with recurrent venous thrombosis. There were 788 individuals in the cohort with venous thrombosis: 357 had factor V Leiden, and 137 had prothrombin G20210A mutation, 27 had factor V Leiden and/or prothrombin G20210A homozygosity, and 49 were double heterozygotes for both mutations. The cohort comprised 463 "controls" with only one venous thrombosis and 325 "cases" with recurrent venous thrombosis. Compared with noncarriers, the crude odds ratio for recurrence was 1.2 (95% confidence interval [CI], 0.9-1.6) for heterozygote carriers of factor V Leiden, 0.7 (95% CI, 0.4-1.2) for prothrombin G20210A, 1.2 (95% CI, 0.5-2.6) for homozygous carriers of factor V Leiden and/or prothrombin G20210A, and 1.0 (95% CI, 0.6-1.9) for double heterozygous of both mutations. Risk estimates were not altered by adjustments for family status, sex, age, other natural anticoagulant deficiencies, or first event type.

Comment: The study has major indications for the evaluation of patients with a first-time unprovoked venous thrombosis. It suggests evaluation for factor V Leiden and prothrombin G20210A mutations have little clinical implication or benefit for the individual with a first-time venous thrombosis. If recurrence of first-time venous thrombosis is not increased by the presence of these mutations, then there is no need to test for them in the patient with an initial unprovoked venous thrombosis. The information in this study does not apply to individuals with multiple recurrent venous thrombi. It is also important to consider, because these mutations are genetic, whether it is still reasonable to perform thrombophilia testing in the patients with first-time venous thrombosis so that family members can be appropriately counseled.

Superficial Venous Thrombosis and Venous Thromboembolism A Large, Prospective Epidemiologic Study

Decousus H, Quere I, Presles E; Prospective Observational Superficial Thrombophlebitis Study Group. Ann Intern Med 2010;152:218-24.

Conclusion: A substantial number of patients with superficial venous thrombosis (SVT) have venous thromboembolism (VTE) at presentation.

Patients with SVT that do not have VTE at presentation can develop this complication in the following 3 months.

Summary: SVT is painful, relatively common, and is thought to have a benign prognosis. However, there is accumulating evidence that SVT often occurs with DVT or pulmonary embolism (PE). DVT appears to be present in about 6% to 53% of patients with SVT and PE in between 0% and 10% of patients with SVT (Leon L et al, Eur J Vasc Endovasc Surg 2005;29:10-7). The authors performed this large observational study to determine the prevalence of concurrent SVT and VTE, to assess how SVT is treated, and to determine the 3-month incidence of thromboembolic complications in patients with SVT. Risk factors for VTE complications in patients presenting with SVT were also determined. This was a national cross-sectional and prospective epidemiologic cohort study performed in France. Office- and hospital-based vascular medical specialists registered with the Societe Franciase de Medecine Vasculaire or Societe Franciase de Phlebologie were invited to enroll patients in the study. To be eligible for the study, patients had to be aged ≥18 years with symptomatic lower extremity SVT. SVT was defined as subcutaneous noncompressible hypoechoic area in the course of an identifiable superficial vein >5 cm in length. Excluded patients were those who had undergone surgery ≤10 days, those where SVT occurred <30 days after sclerotherapy, and those in whom follow-up was not considered feasible. The study included 844 consecutive patients (547 women) with symptomatic lower extremity SVT. Median age was 65 years. At presentation 210 patients (24.9%) also had DVT or symptomatic PE. Of the 600 patients without DVT or PE at study inclusion, and who were eligible for 3-month follow-up, VTE complications developed in 58 (10.2%) at 3 months (PE, 0.5%; DVT, 2.8%; extension of SVT, 3.3%; recurrence of SVT, 1.9%). A total of 540 patients (90.5%) received anticoagulants. Risk factors for complications at 3 months were history of DVT or PE, previous cancer, absence of varicose veins, and male sex.

Comment: The study indicates symptomatic SVT is not necessarily benign. About 25% of the patients will have symptomatic PE or DVT at presentation, and in an additional 10%, some manifestation of VTE or complication of their SVT will develop at 3 months. Given the percentage of patients who present for evaluation of symptoms consistent with SVT and who also have DVT, it would appear prudent to perform a venous ultrasound examination in all patients with suspected SVT. This would appear especially so if anticoagulation is going to be withheld. Patients with identifiable risk factors for development of VTE after SVT and who are not going to be treated with anticoagulation should be considered for follow-up duplex ultrasound imaging.

Vena Cava Filter Occlusion and Venous Thromboembolism Risk in Persistently Anticoagulated Patients: A Prospective, Observational Cohort Study

Hajduk B, Tomkowski WZ, Malek G, et al. Chest 2010;137:877-82.

Conclusion: Patients with inferior vena cava (IVC) filters that are inserted after venous thromboembolism (VTE) who are managed with continued therapeutic anticoagulation have a favorable prognosis when managed with a protocol that includes clinical surveillance, ultrasound examination of the IVC filter, and greater degrees of anticoagulation if a filter clot is detected.

Summary: The authors hypothesized that in patients with IVC filters, anticoagulation indefinitely would be effective in preventing filter occlusion and venous thrombotic complications. They prospectively evaluated the effect of long-term anticoagulation on the frequency of symptomatic venous thromboembolism (VTE) and IVC patency and flow impairment in a cohort of patients with IVC filters. The patients were monitored for clinical recurrence of VTE as well as with serial ultrasound examinations of the IVC filter. They divided the ultrasound examinations into three categories: (1) those that showed no evidence of filter thrombus, (2) those that showed slight inclusion of filter thrombus, with slight inclusion defined as when color Doppler indicated more than half but less than all of the IVC filter to be occluded by thrombus, and (3) large, but incomplete occlusion, was defined when phasic flow modulated by breathing maneuvers was reduced to between 10% and 50% of the IVC filter field. Patients with slight occlusion had frequency of clinic visits and international normalized ratio (INR) determinations increased to approximately weekly, with the target INR of 2.5 unchanged. In patients with larger and complete occlusion, their anticoagulation therapy was switched to low-molecular-weight heparin at therapeutic doses for 5 to 7 days, and then to about 75% of the therapeutic dosage after 1 week. They were monitored by ultrasound imaging every 1 to 2 weeks until the occlusion normalized by ultrasound criteria. At that point they were then transitioned back to oral anticoagulation therapy. The authors also followed a cohort of patients with persistent anticoagulation who did not have IVC filters.

There were 121 patients in the IVC filter cohort under observation. Symptomatic DVT occurred in 24 (20%; 95% CI, 14%-28%). Symptomatic pulmonary embolism (one fatal) was diagnosed in six patients (5%; 95% CI, 2%-10%). There were 45 episodes of filter clot in 36 patients (30%; 95% CI, 22%-38%). There were 30 episodes of slight occlusion, 13 episodes of large occlusion, and 2 episodes of complete filter occlusion. With the management protocol detailed above, all episodes of slight occlusion resolved. The average period of low-molecular-weight heparin treatment in the 15 episodes of large or complete occlusion was 4 to 6 weeks. All instances of large or complete occlusion resolved with the management protocol above. The longest duration until ultrasound resolution of IVC filter complete occlusion was 8 weeks. The rate of major bleeding in the filter cohort was 6.6% and was similar to the 5.8% in patients with persistent anticoagulation without IVC filters.

Comment: The authors are proposing an ultrasound-based follow-up protocol for patients with permanently implanted IVC filters who can be anticoagulated. The data would be more convincing if independent observers had confirmed the IVC filter ultrasound examinations. Nevertheless, the idea of serially monitoring IVC filters and increasing the intensity of anticoagulation or increasing the intensity of monitoring of anticoagulation in response to ultrasound-detected filter clot is interesting. Who will provide such monitoring is a question, but logically, those who perform procedures on patients should be vested in the long-term outcome and monitoring of those procedures.